8

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The P2Y(1) receptor closes the N-type Ca(2+) channel in neurones, with both adenosine triphosphates and diphosphates as potent agonists.

Filippov AK, Brown DA, Barnard EA.

Department of Pharmacology, University College London, Gower Street, London WC1E 6BT. Department of Pharmacology, University of Cambridge, Tennis Court Road, Cambridge CB2 1QJ, UK.

The rat P2Y(1) nucleotide receptor, the P2Y subtype abundant in the brain, was heterologously expressed in rat superior cervical ganglion neurones by micro-injection of the receptor cRNA or cDNA. ADP inhibited the N-type Ca(2+) current by 64%, with EC(50) 8.2 nM, an action blocked competitively by the P2Y(1) receptor antagonist adenosine 3', 5'-bis-phosphate (K(i) 0.7 microM). 2-Methylthio-ADP inhibited the Ca(2+) current likewise, but with EC(50) 0.57 nM, giving the highest potency reported therewith for P2Y(1). Significantly, ATP and 2-methylthio-ATP were also agonists, the latter again at a very high potency (EC(50) 2.5 nM). We propose that this neuronal receptor, when present in brain at a high density as at synapses, can respond to very low concentrations of ATP and ADP as agonists, and that this would result in inhibition of N-type Ca(2+) currents and hence can reduce transmitter release or increase neuronal excitability.

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